(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 703 455 A1

# (12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
**27.03.1996 Bulletin 1996/13**

(51) Int. Cl.[6]: **G01N 35/00**

(21) Application number: **95114811.3**

(22) Date of filing: **20.09.1995**

(84) Designated Contracting States:
**DE FR GB**

(30) Priority: **21.09.1994 JP 226226/94**

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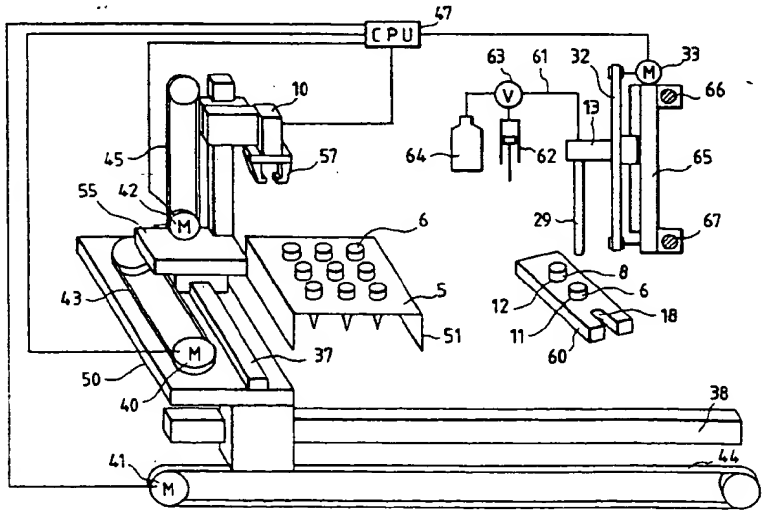
## (54) Analyzing apparatus having pipetting device

(57) An analyzing apparatus comprises a transfer device having a movable gripper (10), a pipetting device having a movable nozzle (29) and a measuring unit (46). One of tips (6) arranged on a tip rack (5) and one of vessels (8) arranged on a vessel rack are held by the gripper (10) to be set in a tip holder (60). A nozzle (29) pushes the tip (6) on the tip holder (60) to connect to the tip (6). A sample and reagents are delivered into a vessel (8) on the tip holder (60) by the tip (6) connected to the nozzle (29). The used tip (6) is detached from the nozzle (29). The vessel (8) containing a reaction mixture is transferred to a sucking position with the gripper (10) after incubation, and the reaction mixture is introduced into the measuring unit. The used vessel (8) is transferred to a waste box with the gripper (10).

FIG. 3




EP 0 703 455 A1

## Description

The present invention relates to an apparatus analyzing a liquid sample such as a biological sample, and more particularly relates to an analyzing apparatus having a pipetting device for transferring a sample from a sample cup to a reaction vessel.

In an automated analyzing apparatus analyzing many kinds of analytical items by reacting a biological sample with reagents, an analyzing apparatus is widely employed of a type in which a row of reaction vessels are transferred with a turntable as disclosed in, for example, Japanese Patent Publication No.6-27743 (1994) and Japanese Patent Application Laid-Open No.6-88828 (1994).

Japanese Patent Application Laid-Open No.6-88828 (1994) in the above patents teaches an immunoassay apparatus which comprises a reagent unit having a turntable arranging reagent bottles, a sample transfer unit for transferring a sample rack to a sample pipetting position on the transfer path, a reagent delivery unit for delivering reagents from the reagent unit to a reaction table, and a sample delivery unit for deliver a sample from the sample rack to the reaction table.

On the other hand, a sample delivery apparatus without turntable is disclosed in Japanese Patent Application Laid-Open No.4-296655 (1992). In this conventional technology, test tubes which are empty, sample cups and nozzle tips are arranged on an X-Y stage, and the disposable nozzle tip is connected to a nozzle communicated with a pump, and then a sample is delivered from the sample cup to the test tube.

The inventors of the present invention have tried to realize an automated analyzing apparatus using disposable nozzle tips and disposable reaction vessels. However, when the same method of delivering tip as in Japanese Patent Application Laid-Open No.4-296655 (1992) is employed in this analyzing apparatus, it is necessary to connect the tip to the nozzle on the tip array region on the X-Y stage.

In this case, since a pushing force is applied against the tip rack when the tip is connected to the nozzle, the tip rack needs to have a strong structure. If an operator of the analyzing apparatus reuses the tip rack, it arises troublesome work to arrange many tips on the tip rack by hand. On the other hand, if the tip rack having a strong structure is thrown out, extra cost is required.

An object of the present invention is to provide an analyzing apparatus capable of properly performing to connect tip to a nozzle of a delivery device without forming the tip rack for arranging many nozzle tips in a strong structure.

Another object of the present invention is to provide an analyzing apparatus capable of decreasing consuming number of disposable tips by using one disposable tip and delivering one sample and a plurality of reagents.

An analyzing apparatus according to the present invention comprises a tip rack for arranging a plurality of nozzle tips, a pipetting device for transferring a liquid sample from a sample cup to a reaction vessel using a disposable nozzle tip connected to a nozzle in a first predetermined region, a tip holder provided in the first predetermined region, a tip gripper movable in a second predetermined region, and a transfer device for transferring a nozzle tip on the tip rack to the tip holder using tip gripper.

The disposable tip transferred by the tip gripper is connected to the nozzle of the pipetting device by pushing the nozzle tip to the nozzle on the tip holder. Therefore, the tip holder is made of a material having a stiffness large enough to endure the pushing force of the nozzle. However, since the tip rack having a lot of nozzle tips arranged does not receive the pushing force, the tip rack is made of a material of low strength which is capable of supporting the tips. In this case, the tip rack is preferably a thin molded plastics. The tip rack has many tip insertion holes arranged in a given interval in the X-direction and Y-direction so that positions of a large number of tips are accurately determined. Such tip racks in a state of tips inserted are supplied from a vendor. Thereby, it is no need for a user to do work to set many tips on a tip rack.

In a preferable embodiment, the tip holder comprises a tip connecting station, a sample receiving station and a tip detaching station. The nozzle tip connected to the nozzle at the tip connecting station is cleaned with the cleaning unit after a reagent is transferred to the reaction vessel. The nozzle tip after cleaned transfers a sample to the reaction vessel, and then is detached from the nozzle at the tip detaching station.

Embodiments of the present invention will now be described, by way of example, with reference to the accompany drawings in which:

FIG.1 is a view showing the outward appearance of one embodiment of an analyzing apparatus in accordance with the present invention,
FIG.2 is a schematic plane view of the analyzing apparatus of FIG.1,
FIG.3 is a schematic view explaining the operation of the analyzing apparatus of FIG.1, and
FIG.4 is a view explaining the state of connecting a tip to a nozzle in a pipetting device.

An embodiment according to the present invention will be described below, referring to FIG.1 to FIG.4.

In FIG.1, a sample supplying device has a turntable 1 on which many sample cups are arranged. A reagent positioning device has a turntable 3 on which reagent bottles corresponding to plural analytical items are arranged. In a rack supplying area, three tip racks 5 and three vessel racks 7 are placed. A transfer device has a fixed rail 38, a rail 37 movable on the rail 38, and a movable gripper 10 moving on the rail 37.

A pipetting device has a movable member 13 and a pipetting nozzle 29 supported by the movable member 13. An incubator unit 9 heats a plurality of reaction vessels containing mixtures of a sample and a reagent at a certain temperature, for example 37°C. A measuring unit

46 has a flow cell and an optical system for measuring a reaction liquid in the flow cell. A tube 49 for sucking the reaction liquid is suspended from a movable arm 14. A reaction liquid sucked by the sucking operation of a syringe mechanism 48 through a tube 49 is introduced into the flow cell of the measuring unit 46 to be measured. The reaction liquid after measured is collected in a waste tank 20. A control unit 47 controls operation of each mechanism in the analyzing apparatus.

In FIG.2, on the turntable 1 there are arranged many sample cups 2 containing biological samples such as blood or urine. The turntable 1 is intermittently rotated to position each of the sample cups 2 at a sucking position 27. On the turntable 3 there are arranged many reagent bottles 4. The reagent bottle 4 has three rooms 21, 22, 23. The reagent bottle 4 is placed so that a first reagent room 21 comes in the inner peripheral side. Therefore, when all the reagent bottles are set, three concentric circles are formed around the center of the rotation. That is, a row of the first reagent rooms 21 is formed along the innermost concentric circle, a row of the second reagent rooms 22 is formed along the intermediate concentric circle, and a row of the third reagent rooms 23 is formed along the outermost concentric circle. As the turntable 3 is intermittently rotated, the first reagent room 21 is positioned at a sucking position 24, the second reagent room 22 is positioned at a sucking position 25, and the third reagent room 23 is positioned at a sucking position 26.

Three tip racks 5 are mounted on a rack supplying area in the moving region of the gripper 10. Beside the three tip rack 5, three vessel racks 7 are mounted. In each of the tip racks 5, tip insertion holes spacing in an equal interval are formed in the X-direction and in the Y-direction. A nozzle tip 6 has a nearly conical thin tube with a jaw 52 held by the gripper 10 as shown in FIG.4. The nozzle tip 6 is formed of a resin such as polypropylene. The tip rack 5 is a thin molded plastics and has legs 51. The tip rack 5 is formed of a resin such as polypropylene. Many unused nozzle tips 6 are mounted on the tip rack 5.

The structure of the vessel rack 7 is the same as that of the tip rack 5. The reaction vessel 8 is a molded plastics with a jaw 53 held by the gripper 10 as shown in FIG.4.

The incubator 9 in FIG.2 has a thermal-conductive metal member and a heating unit for heating the metal member at a given temperature. In the metal member, there are formed a plurality of holes into which the reaction vessels are inserted. These holes are open upward.

In FIG.2 and FIG.3, a transfer device for selectively transferring the nozzle tip and the reaction vessel has the rail 38 extending in the Y-direction. A base 50 having the rail 37 extending in the X-direction is connected to a belt 44 and moved on the rail 38 in one direction or the opposite direction with the belt 44 rotated by a motor 41 controlled by the control unit 47.

The base 50 has a motor 40 for rotating a belt 43. A base 55 is slidably attached to the rail 37 on the base 50. The base 55 is connected to a belt 43 and moved on the rail 37 in the longitudinal direction of the rail 37 by rotation of the motor 40. the base 55 has a motor 42 for rotating a belt 45 and a vertical rail 39.

The movable gripper 10 is slidably attached to a vertical rail 39, and moved upward and downward according to Morton of the belt 45. The movable gripper 10 has a pair of reclosable claws 57 capable of gripping either the nozzle tip 6 or the reaction vessel 8. The operation of releasing and gripping of the pair of claws 57 is controlled by the control unit 47.

The movable gripper 10 grips up the unused tip 6 on the tip rack 5 one-by-one using the claws 57 to transfer it to a tip holder 60, and releases gripping of the tip 6 after inserting the tip 6 into a hole of the tip connecting station 11 in the holder 60. Further, the movable gripper 10 grips up the unused vessel 8 on the vessel rack 7 one-by-one using the claws 57 to transfer it to a tip holder 60, and releases gripping of the vessel 8 after inserting the vessel 8 into a hole of the sample receiving station 12 in the holder 60. These operations are repeated every interval of a given period.

As shown in FIG.3, FIG.3 and FIG.4, the sample receiving station 12, the tip connecting station 11 and the tip detaching station 18 on the tip holder 60 are linearly arranged along the horizontal moving locus 34 of the nozzle 29 of the pipetting device. The tip cleaning position 17, the reagent sucking positions 24, 25, 26 and the sample sucking position 27 are arranged along the horizontal moving locus 34 of the nozzle 29. The locus 34 passes through an area off from the rotating center of the turntable for reagents and linearly passes across the three concentric circles. The tip holder 60 receiving the tip 6 and the vessel 8 from the movable gripper 10 is installed in an area overlapped with the movable region of the movable gripper 10 and the movable region of the nozzle 29 of the movable member 13.

The movable member 13 of the pipetting device is, as shown in FIG.3, connected to a belt 32 rotated between a pair of pulleys driven by a motor 33 to travel upward and downward according to motion of the belt. The nozzle 29 supported to the movable member 13 is connected to a syringe pump 62 through a conduit 61. The pump 62 is connected to a cleaning tank 64 through a switching valve 63. A slider 65 having the movable member 13 and the motor 33 is horizontally moved along a pair of rails 66, 67. As shown in FIG.2, the slider 65 is connected to a belt 30 and horizontally moved by rotation of the belt 30 driven by a motor 31.

After the disposable tip 6 is put in the tip holder 60 by the movable gripper 10, the motor 33 is started to drive based on a command of the control unit 47 to move the movable member 13 downward. As shown in FIG.4, the end of the nozzle 29 moved down is inserted into the tip 6. By pushing down the nozzle further, the outer wall of the nozzle 29 is tightly connected to the inner wall of the tip 6. Therefore, the pushing force from the nozzle 29 is applied to the tip holder 60. The tip holder 60 is made of

a material endurable against such a pushing force, for example, stainless steel plate of 8 mm thickness.

When the nozzle 29 is moved upward as the motor 33 drives, the tip 6 connected to the nozzle 29 is also moved upward together. After the tip delivers the reagents from the reagent bottles 24, 25 and 26 and the sample from the sample cup 2 to the reaction vessel 8, the tip 6 finishing its role is transferred to the tip detaching station 18 of the tip holder 60. The tip 6 is moved downward and in the lateral direction so that the upper portion of the jaw 52 of the tip 6 touches to the lower portion of the station 18 by motion of the nozzle 29. Then the nozzle 29 is moved upward to hook the upper portion of the tip to the tip holder 60 and the tip 6 is detached from the nozzle 29.

A box 15 for receiving waste having a size extending over the vessel rack supplying area and the tip holder 60 is placed below. A collecting bag made of vinyl chloride is set inside the box 15. The used tip 6 detached at the tip detaching station 18 is dropped and collected in the bag. There is a vessel throwing-out hole 19 opened on the top of the box 15. The used reaction vessel 8 after sucked the reaction liquid at the reaction liquid sucking position 28 is gripped by the movable gripper 10 and transferred from the sucking position 28 to the throwing-out hole 19. Then the gripper 10 is released on the hole 19 to drop the used vessel 8 into the box 15. In order to collect the waste, all that an operator has to do is to exchange the bags. Therefore, the operator can manage with touching neither the used tips 6 nor the used vessels 8.

The sucking tube 49 supported by the movable arm 14 is moved both horizontally and vertically. The tube 49 is lowered into the reaction vessel 8 placed at the sucking position 28, and the reaction liquid is conducted to the flow cell of the measuring unit 46 by operation of the syringe mechanism 48. Then the tube 49 is moved upward and transferred onto a cleaning solution bottle 36. After the tube 49 is moved down and the cleaning solution is conducted to the flow cell through the tube 49, the tube 49 is moved upward and transferred onto a buffer solution bottle 35. The tube 49 is moved downward and a buffer solution is conducted to the flow cell through the tube 49. Then the tube 49 is moved upward and transferred to the sucking position 28 for the next reaction liquid. The various kinds of solutions passed through the measuring unit 46 are collected into the waste liquid tank 20.

Operation of an automated analyzing apparatus will be described below.

The nozzle tips 6 are supplied by a vendor in a state of being arranged in the tip rack 5. The unused reaction vessels 8 are also supplied by a vendor in a state of being arranged in the vessel rack 7. An operator mounts such a tip rack 5 and such a vessel rack 7 on the tip supplying area. The sample cups 2 containing samples to be analyzed are arranged on the turntable 1, and reagent bottles 4 corresponding to analytical items are arranged on the turntable 3.

The movable gripper 10 is moved onto the tip rack 5 and moved down with the claws 57 kept open to grip one of nozzle tips 6 at the jaw 52 by closing operation of the claws 57. The gripper 10 is moved upward in keeping the state as it is and then is horizontally moved to transfer the nozzle tip 6 to the tip holder 60. The tip 6 is placed at the tip connecting station 11 by the gripper 10 and released from the gripper 10 by opening operation of the claws 57. The nozzle 29 is moved down to the tip connection station 11, and the nozzle 29 is connected to the tip 6 by pushing the tip 6 with the nozzle 29.

Then the nozzle 29 is moved upward and the tip 6 connected to the nozzle 29 is horizontally moved toward the sucking position 24 on the turntable 3. During that time, the movable gripper 10 is moved onto the vessel rack 7 and grips one of the vessels 8 at the jaw 53 of the vessel 8 to place it to the sample receiving station 12 of the tip holder 60.

A given amount of the first reagent is sucked with sucking operation of the pump 62 into the tip 6 which is moved down into the first reagent room 21 positioned at the sucking position 24. The tip 6 having the first reagent is moved upward and horizontally moved to the sample receiving station 12. The reagent is delivered from the tip 6 moved down to the station 12 into the vessel 8. Then the tip 6 is moved upward to transferred to the cleaning tank 17. The cleaning tank 17 is supplied with cleaning solution from the cleaning unit 16. The tip 6 is cleaned in the cleaning tank 17.

During cleaning of the tip 6, the turntable 3 is rotated to position the second reagent room 22 on the intermediate concentric circle to the sucking position 25. The cleaned tip 6 is inserted into the reagent room 25 of the sucking position 25 to suck a given amount of the second reagent. The upward moved tip 6 is transferred to the sample receiving station 12 to deliver the second reagent into the vessel 8. Then, the tip 6 is cleaned in the cleaning tank 17. The turntable 3 moves the third reagent room 23 in the outermost circle to the sucking position 26. The third reagent sucked in the tip 6 is delivered into the vessel 8 on the station 12. The nozzle tip 6 having delivered the reagent is again cleaned in the cleaning tank 17. The cleaned tip 6 is moved to the sucking position 27 of the turntable 1, and moved down into the sample cup 2 positioned at position 27. A given amount of the sample is sucked into the tip 6 by operation of the pump 62. The tip 6 is upward and horizontally moved, and moved downward at the sample receiving station 12 of the tip holder 60 to deliver the sample in the tip 6 into the reaction vessel 8 already containing the reagents.

The tip 8 after finishing delivery of the reagent and the sample is transferred to the detaching station 18 to be detached from the nozzle 29. The reaction vessel 8 containing the mixture of the sample and reagent is gripped by the movable gripper 10 at the jaw 53 to be inserted into a vacant receiving hole in the incubator 9 and released from the gripper 10. The vessel 8 is incubated at a constant temperature for a given time period determined depending on the analytical item. In the incu-

bator 9, reactions of plural samples are proceeded in parallel. The reaction vessel 8 passed the given reaction time is lifted by the gripper 10 to be set in the sucking position 28. The reaction liquid sucked from the tube 49 is conducted to the flow cell of the measuring unit 46. The vacant vessel 8 is gripped by the gripper 10 at the sucking position 28 and transferred to the throwing-out hole 19 to be thrown out.

During the time when the vessel 8 is staying at the incubator 9, the transfer device transfers a disposable tip 6 and a vessel 8 for the next sample to the tip holder 60, and the pipetting device performs pipetting operation of the reagent and the sample. By repeating supplying operation of the tip 6 and the vessel 8 using the movable gripper 10, when all the tips 6 on the rack 5 and all the vessels 8 on the rack 7 are used, the analyzing apparatus completes the analyzing operation.

According to the aforementioned embodiment, since the apparatus is constructed so that the tip 6 is connected to the nozzle 29 at the tip holder 60 and only the work to lift and draw out the tip 6 using the movable gripper 10 is performed at the tip rack, no excessive force is applied to the tip rack. Therefore, the tip rack can be formed of a material as comparatively low a strength as the tip rack can support many tips spacing one another. Since such a tip rack is supplied by vendor in a state where many tips are orderly arranged, it is unnecessary for an operator to arrange the tips in the tip rack.

Since work done by the transfer device and work done by the pipetting device can be performed in parallel, a high analyzing efficiency can be attained. Since a sample and reagents are pipetted using a single disposable tip, consumed number of tips can be decreased. Since both of the tip connecting station and the sample receiving station are installed in a place where the movable region of the gripper 10 and the movable region of the nozzle 29 are overlapped, the analyzing apparatus can be made small.

## Claims

1. An analyzing apparatus having a pipetting device for transferring a liquid sample from a sample cup (2) to a reaction vessel (8) using a disposable nozzle tip connected to a nozzle (29), said nozzle being movable in a first given region, which comprises:

   a tip rack (5) for arranging a plurality of nozzle tips;

   a tip holder (60) provided in said first given region;

   a tip gripper (10,57) movable in a second given region; and

   a transfer device for transferring a nozzle tip on said tip rack to said tip holder using said tip gripper.

2. An analyzing apparatus according to claim 1, wherein said pipetting device connects said nozzle tip held on said tip holder by pushing said nozzle against said nozzle tip to said nozzle.

3. An analyzing apparatus according to claim 2, wherein said tip holder is made of a material having a stiffness endurable to the pushing force of said nozzle.

4. An analyzing apparatus according to claim 3, wherein said tip rack is a molded plastics having a plurality of tip insertion holes arranged in a given interval.

5. An analyzing apparatus according to claim 2, wherein said tip holder comprises:

   a tip connecting station (11) at which said held nozzle tip is connected to said nozzle of said pipetting device;

   a sample receiving station (12) at which a sample delivered from said connected tip is received by a reaction vessel; and

   a tip detaching station (18) at which said connected nozzle tip after said sample is delivered is detached from said nozzle.

6. An analyzing apparatus according to claim 5, wherein said tip connecting station, said sample receiving station and said tip detaching station are arranged in said first given region in a straight line (34).

7. An analyzing apparatus according to claim 5, wherein a bag for collecting used nozzle tips is provided below said tip detaching station.

8. An analyzing apparatus according to claim 5, wherein

   a tip cleaning unit (16,17) is provided in said first given region, said connected nozzle tip being cleaned with said cleaning unit after a regent is transferred to said reaction vessel, transferring a sample to said reaction vessel after cleaning, and then being detached from said nozzle at said tip detaching station.

9. An analyzing apparatus according to claim 2, which comprises a reagent positioning device arranging reagent containers (4) along each of plural concentric circles on a turntable (3) and a sample supplying device (1) for supplying a sample cup (2) to a sample sucking position (27), said nozzle of said pipetting device being moved so as to cross said plural concentric circles off the rotating center of said turntable of said reagent positioning device and further being linearly moved above said tip holder, said reagent positioning device and said sample supplying device.

10. An analyzing apparatus according to claim 9, which comprises a vessel rack (7) for arranging a plurality of unused reaction vessels (8), and an incubator unit (9) for keeping a reaction vessel (8) receiving a sample and a reagent at a given temperature so as to incubate an mixture thereof, said transfer device transferring a reaction vessel (8) on said vessel rack to said tip holder using said gripper as well as transferring a reaction vessel receiving a sample and a reagent on said tip holder to said incubator unit using said gripper.

11. An analyzing apparatus according to claim 10, which comprises introducing means for introducing a reaction solution from a reaction vessel (8) placed at a reaction solution sucking position (28) to a measuring device (46), said transfer device transferring said reaction vessel by which said incubated mixture is received from said incubator unit to said reaction solution sucking position using said gripper.

12. An analyzing apparatus according to claim 2, wherein said tip holder is installed in a region overlapped by said first and second given regions.

FIG. 1

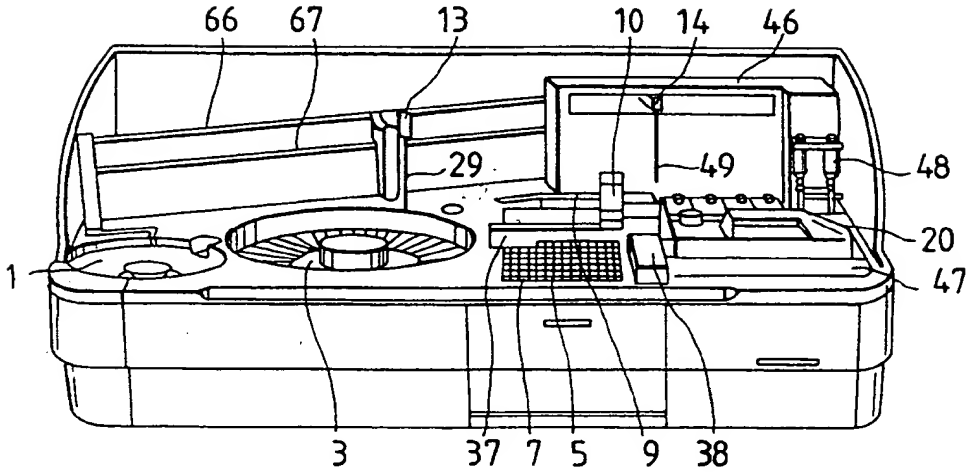



FIG. 4

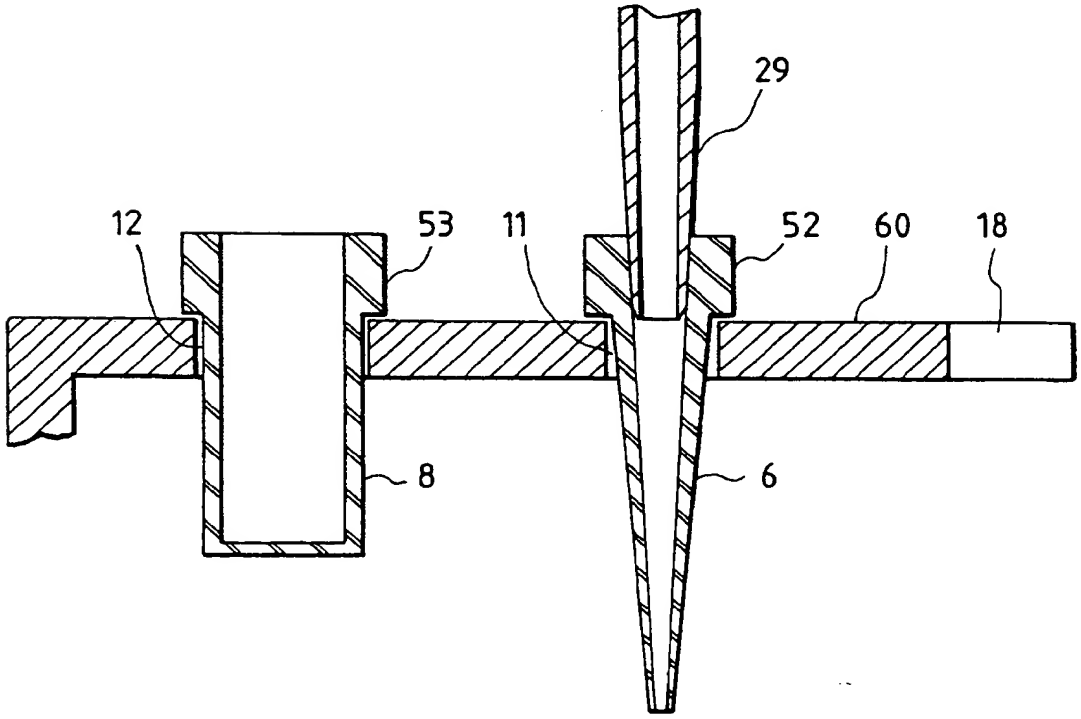


FIG. 2

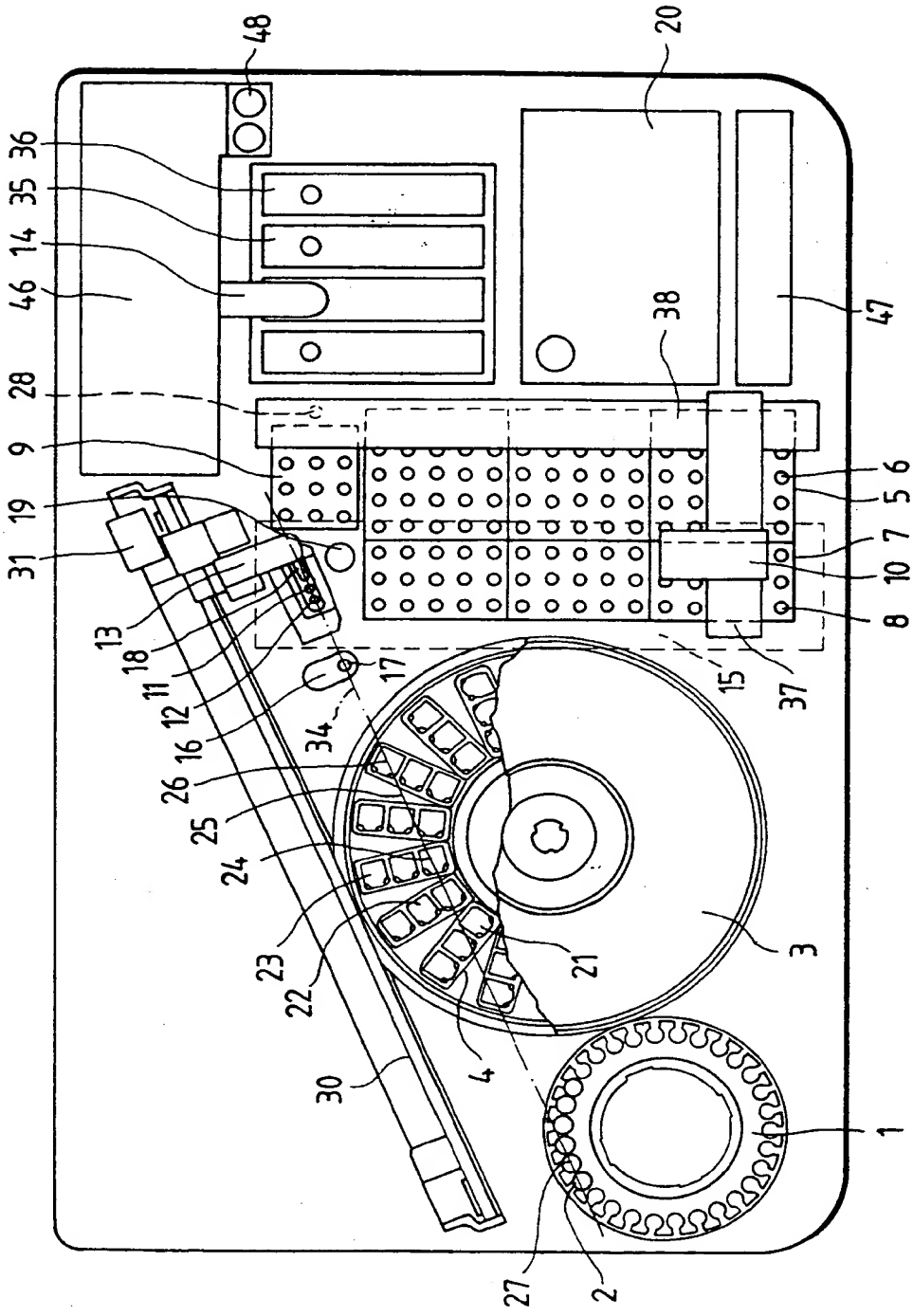
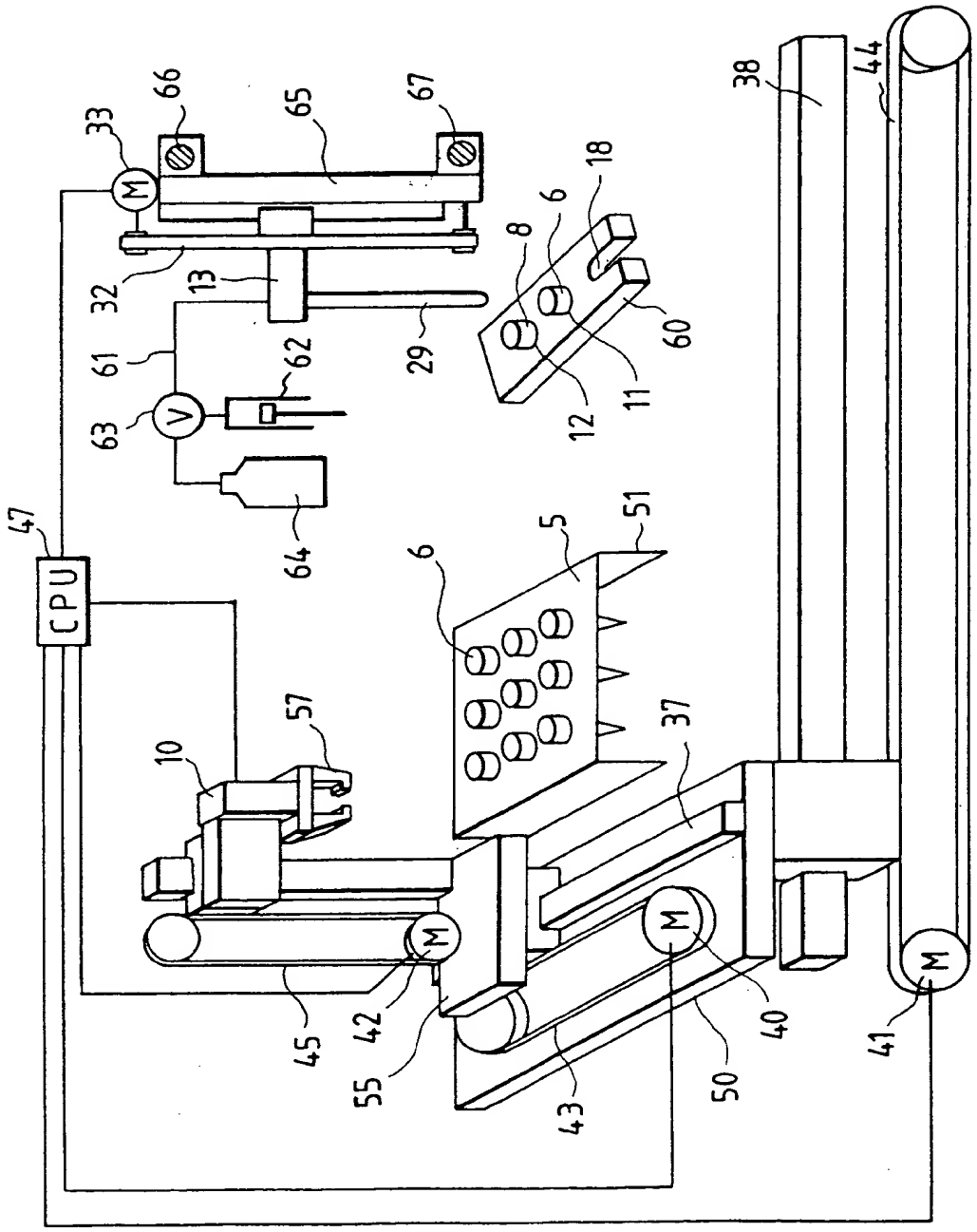


FIG. 3



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# EUROPEAN SEARCH REPORT

Application Number
EP 95 11 4811

## DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (Int.Cl.6) |
|---|---|---|---|
| A | PATENT ABSTRACTS OF JAPAN<br>vol. 9 no. 50 (P-339) ,5 March 1985<br>& JP-A-59 188538 (NIHON NUNKOU KOGYO KK)<br>* abstract * | 1 | G01N35/00 |
| A | DE-A-43 06 332 (MANNESMANN)<br>* column 2, line 25 - line 42; figure 1 * | 1 | |
| A | US-A-4 087 248 (MILES)<br>* column 10, line 18 - line 37; figure 7 *<br>* column 10, line 45 - line 64 * | 2,3 | |
| A | EP-A-0 282 076 (SUMITOMO)<br>* column 9, line 10 - column 10, line 51; figures 10-16 * | 2,3 | |
| A | DE-A-37 33 098 (HITACHI)<br>* claim 6; figures 9A-9P * | 5,7 | |
| A | EP-A-0 557 828 (HORIBA)<br>* column 4, line 45 - column 5, line 35; figures 1-7 * | 1 | |
| | | | TECHNICAL FIELDS SEARCHED (Int.Cl.6)<br>G01N |

The present search report has been drawn up for all claims

| Place of search | Date of completion of the search | Examiner |
|---|---|---|
| THE HAGUE | 11 December 1995 | Hocquet, A |

CATEGORY OF CITED DOCUMENTS

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